ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

Location of Meeting
Frontier Building, 3601 C Street, Room 890/896

FINAL- MINUTES OF MEETING
September 15, 2006
8:00 a.m.

Committee Members Present:
Marvin Bergeson, MD
Heidi Brainerd, MS, RPh
Amber Briggs, PharmD
Richard E. Brodsky, MD
Robert Carlson, MD
Kelly Conright, MD
Jeffrey G. Demain, MD
Traci Gale, RPh
Vincent Greear, RPh (telephonic)
R. Duane Hopson, MD
Thomas K. Hunt, MD
Diane Liljegren, MD (telephonic)
Andrzej Maciejewski, MD
Ronald J. Miller, RPh
Gregory R. Polston, MD
Sherrie Richey, MD
Janice L. Stables, MSN, ANP
George Stransky, MD
Alexander H. vonHafften, MD (telephonic)
Trish D. White, RPh (telephonic)

Committee Members Absent:
Michale Boothe, DDS
Ronald Keller, MD

Others Present:
David Campana, RPh
Melinda Sater, PharmD, First Health

1. Call to Order – Chair

The meeting was called to order at 8:05 a.m.

2. Roll Call

A quorum was present.

3. Public Comment – Local Public/Local Physicians

Dr. Jeremy Gitomer: Via teleconference, Mr. Gitomer discussed the electrolyte depleters used in dialysis and pre-dialysis patients – RenaGel, Fosrenol and PhosLo. Fifteen to 20% of patients have side effects so we frequently have to switch drugs or use combination drugs. Ninety percent of the patients use RenaGel and PhosLo. Regarding statins, it is now estimated that 15% of the general population has chronic kidney disease. The American Heart Association recommends a LDL cholesterol level of 70, because the relative risk of heart attacks for age match control, without kidney disease, increases from three-fold to a thousand-fold depending on age. The average LDL cholesterol level of 35 of my patients, prior to the initiation of statin therapy, was 146 in March. A 60% reduction will probably not be achieved unless Crestor and Lipitor are used. Atorvastatin should be placed on the formulary.

4. Re-review of Alpha Blockers

Dr. Stephanie Greenstein: Discussed benign prostatic hyperplasia (BPH), a common disease in aging men. Most symptoms rarely occur before the age of 40. Greater than 50% of men in their 60s, but as many as 90% in their 70s and 80s, have symptoms of BHP. Approximately 26% of men, age 40 to 49, have moderate to severe urinary tract systems, which increases to 46% in men in their 70s. BPH increases risk factors for acute urinary retention and sexual dysfunctions. Trials on Flomax have shown sustained improvements in symptoms and quality of life. Flomax was generally well tolerated and adverse events were usually mild. Long-term data has indicated that no new adverse events occur with long-term use. Patients receiving Flomax reported a low incident of clinically significant hypertension. While Flomax treated patients reported a somewhat higher rate of abnormal ejaculation, they experienced overall improvement in sexual function. Flomax does not interact with common medications, including several antihypertensives. Patients with mild to moderate renal insufficiency and hepatic impairments can tolerate Flomax. Additionally, there are no cautions on the label against use for patients with cardiac problems. In a randomized, double-blind, multicenter study, 625 patients with BPH were randomized to receive Alfuzin 10 and 15 milligrams versus Flomax 0.4 milligrams and placebo. The number of adverse events was low across all study groups. Dizziness occurred in 7% of patients using Alfuzosin, but less than 2% of the Flomax patients. The number of adverse events affecting ejaculation failure and disorder were low and equal among the groups even though the Flomax dosage was smaller. Flomax is dosed once daily and does not require penetration. No clinically significant hypertension or cardiovascular events were observed during trials. Overall, Flomax demonstrates rapid onset efficacy, proven long-term safety, minimal side effects and gentler drug interactions.

Dr. Sater gave the First Health presentation on the alpha-blockers in the BPH class. There are four available entities, five available products. Cardura is available both as an immediate release and extended release product. All products are FDA approved for the treatment of BPH. Only Cardura and Hytrin are indicated for hypertension. The drugs show similar clinical efficacy and adverse drug reaction profiles, however there are fewer cardiovascular affects with Flomax and Uroxatral due to the receptor's specificity. In August (in Alaska) there were 168 claims for drugs in this class. Flomax, Uroxatral, Teraosin and Doxazosin are currently preferred. At the last meeting there was a brief discussion about how much Flomax was used in Alaska and no other comments. Dr. Kevin Tomera feels Flomax and Uroxatral are therapeutically equivalent and at least one should be on the PDL. He

also stated Flomax was useful for treating renal stones in female patients. The recommendation is class effect.

Dr. Conright felt one drug, which is not also used for the treatment of hypertension, should be preferred. Dr. Liljegren agreed, because a large percentage of patients prescribed these drugs have an increased risk for cardiovascular disease. Dr. Carlson pointed out that the AUA guidelines indicated a class effect. Dr. Conright felt there needed to be an option to treat BPH without treating hypertension. Dr. Carlson pointed out that any drug could be prescribed by writing "medically necessary" on the prescription. Mr. Campana noted that calling this a class effect would put the drugs that came out with a better supplemental rebate, as well as the generics, on the list. Dr. Demain suggested placing one of each on the list as a safety net.

DR. HUNT MOVED THAT THE ALPHA BLOCKERS WERE A CLASS EFFECT AND AT LEAST ONE OF THE NON-CARDIO SELECTIVE AGENTS, FLOMAX OR UROXATRAL, BE INCLUDED ON THE PDL. DR. DEMAIN SECONDED.

MOTION CARRIED UNANIMOUSLY.

5. Re-review of the Androgen Hormone Inhibitors

There was no public comment on this class.

Dr. Sater gave the First Health presentation on the Androgen Hormone Inhibitors. There are two available products, both of which are FDA approved for the treatment of BPH. They have similar pharmacokinetic and clinical efficacy profiles. In Alaska there were only 24 claims in August: Avodart, 67%; and Proscar, 33%. Proscar is currently the preferred agent. Since we reviewed this class, Proscar has been made available in generic form. Dr. Kevin Tomera uses 90% Avodart in his practice, because he feels it is a clinically superior product.

Ms. White asked what happened when patients were switched from one product to another. Dr. Sater said that according to Dr. Tomera if a person was to switch from Proscar to Avodart there would be no clinical effect, because of the more rapid onset of the product. However, switching from Avodart to Proscar could cause a small renal effect, because of the delayed onset of that product.

DR. HUNT MOVED THAT AVODART AND PROSCAR BE CONSIDERED CLASS EFFECT. SECONDED BY DR. BERGESON.

MOTION CARRIED WITH TWO OPPOSED.

6. Re-review of Electrolyte Depletors

There was no public comment on this class.

Dr. Sater gave the First Health presentation on the Electrolyte Depletors, which include PhosLo, RenaGel and Fosrenol. All three agents are FDA approved for the treatment of elevated phosphate

levels and renal disease. In August (in Alaska) there were 54 claims for drugs in this class: PhosLo, 76%; RenaGel, 24%; and no claims for Fosrenol. All agents are currently preferred. The last recommendation was that this was a class effect.

Dr. Maciejewski said RenaGel was a very potent agent and the most utilized. It is filled with calcium, which is often desired. However, we need options, because calcium should not be administered during hypercalcaemia.

DR. MACIEJEWSKI MOVED TO ADD RENAGEL AND PHOSLO TO THE PDL. SECONDED BY DR. DEMAIN.

MOTION CARRIED UNANIMOUSLY.

7. Re-review of Lipotropic - Fibric Acid

Dr. Himanshu Paudric: TriCor is indicated in adult patient with mixed dyslipidemia or primary hypercholesterolemia to increase HDL. There are greater benefits seen in patients with mixed dyslipidemia versus statins alone and in combinations. TriCor has shown that there is a benefit in decreasing some of the emerging biomarkers, which are being looked at aggressively. TriCor 145, a new NanoCrystal technology, can be taken with or without food. The dosage of TriCor 145 is significantly lower than other agents. TriCor has a large body of evidence in terms of side effect data. Abbott Laboratories has provided unsurpassed support to local physicians. Providing samples allows the physicians, as well as the patients, to assess toleration and response. Abbott Laboratories is a leader in providing medical education and answering questions regarding treatment with TriCor. They also have an excellent patient education program. A one-year cost analysis showed a savings of almost $16,400 per 100 patients. TriCor has an unsurpassed safety profile when used in combination with statins.

Dr. Carlson asked what effect TriCor had on total mortality. Mr. Paudric said the FIELD (Fenofibrate Intervention and Event Lower in Diabetes) data shows a slight increase in mortality, however that mortality increase was not statistically significant in a 10,000-patient population. Other studies had varying results, so there no conclusive evidence on total mortality.

Dr. Demain asked about recent concerns with rhabdomyolysis. Dr. Paudric said data presented in the American Journal of Cardiology showed that fenofibrate, combined with statins, was safer in terms of rhabdomyolysis, because it is not metabolized through the same pathway as the statin.

Dr. Hunt asked if there was a head-to-head trial between TriCor and TriCor 145. Dr. Paudric said there was no head-to-head major comparison between the two. Patients are more compliant with TriCor 145, because it does not have to be taken with food.

Dr. Sater gave the First Health presentation on the Lipotropic - Fibric Acid. There are two available entities: four branded and one generic fenofibrate and generic gemfibrozil. In August, in Alaska, there were 203 claims with gemfibrozil at 48% and TriCor at 52%. Both products are preferred. Previous discussions indicated there were fewer drug interactions associated with fenofibrate. The motion was

that those agents be preferred. There have not been significant changes in this class since the last review.

Dr. Hunt asked if TriCor had been selected as the preferred agent at the last review. Dr. Sater said one fenofibrate and one gemfibrozil was preferred. TriCor had not been preferred by name. Three of the branded fenofibrate products can be taken without regard to food. Dr. Hunt asked if bioavailability was substantially increased for drugs that could be taken without food. Dr. Sater said the bioavailability increased by 30%. Dr. Conright asked if the other medications had to be taken with food 100% of the time. Dr. Greear said the labels indicated they should be taken with food.

Dr. Carlson discussed overall mortality. The drug should be selected based on a particular chemical and not by brand. It would be very powerful if a brand could show an improvement in overall mortality.

DR. STRANSKY MOVED THAT ONE GEMFIBROZIL AND ONE FENOFIBRATE BE INCLUDED ON THE PDL. SECONDED BY DR. MILLER.

Dr. Hunt noted that within the fenofibrate class some of the drugs could be taken without food. We have historically favored products for their ease of compliance or dosing, although that does not mean it produces better all cause mortality. The board discussed this issue.

MOTION CARRIED UNANIMOUSLY.

8. Re-review of Lipotropics - Niacin

There was no public comment on this class.

Dr. Sater gave the First Health presentation on Lipotropics - Niacin. There are many products available over the counter. Niaspan and Omacor are the only available prescription products. In August, in Alaska, there were only 23 claims. Both Niaspan and Omacor are preferred. However, Niaspan has 100% market share. There was no previous discussion. The motion was that it was a class effect. There have been no significant changes in this class since last year.

DR. DEMAIN MOVED THAT THIS BE CONSIDERED A CLASS EFFECT. SECONDED BY DR. BERGESON.

MOTION PASSED UNANIMOUSLY.

Dr. Sater said the Omega 3 acid product was not currently a PDL class. However, there was one claim.

Dr. Hunt asked when a drug graduated to a PDL class. Dr. Sater said a PDL class is based on the manufacturers' willingness to submit bids and the cost savings that can be generated around the class.

9. Zetia

Dr. An Pham: Vytorin and Zetia are critical options for first line treatment of hypercholesterolemia. Reducing LDL-C to below 70 is now recommended. Zetia blocks absorption of cholesterol in intestines. Studies have shown remarkable therapeutic success in lowering LDL-C as much as 70%. Vytorin is available in a once a day tablet. Vytorin is the first and only first line lipid-lowering agent approved to simultaneously treat primary sources of cholesterol; first by inhibiting the production of cholesterol in the liver and second by blocking the absorption of cholesterol in the small intestines. The complimentary mechanism of Vytorin reduces LDL-C by 52%. Several large outcome trials are underway to assess the additional benefit of Vytorin on cardiovascular morbidity and mortality. Vytorin was found to be well tolerated. Patients will likely adhere to a medication that is simple to take. Vytorin, in a single tablet, offers superior lipid lower efficacy.

Dr. Demain asked if there was a higher risk with ZoCor or Vytorin with rhabdomyolysis. Dr. Pham said there was no additional warning or risk that was found in clinical studies.

Dr. Sater gave the First Health presentation. There is a single entity in this class, which is also available in a combination. The following discussion is related to Vytorin with statins. Both ezetimibe and the combination are approved the treatment of hypercholesterolemia. Alone, Zetia will decrease LDL by about 18%. In August, in Alaska, there were 176 claims for Zetia. The previous discussion centered on Vytorin. There have not been significant changes in this class since the last review.

Dr. Carlson asked if there was any mortality data that would be coming out in the near future. Dr. Pham said there were a number of studies being conducted, but they are not currently available.

Dr. Hunt asked for a review on the policy regarding combination products. Dr. Sater said combination products are not specifically discussed. If the entities contained in the combination are added to the PDL then the combination will be added if it is cost effective or cost neutral.

DR. BERGESON MOVED TO ADD ZETIA TO THE PDL. SECONDED BY DR. CARLSON.

MOTION PASSED UNANIMOUSLY.

10. Re-review of Statins

Dr. Kris Norenberg: Reviewed the trials being conducted by Astrazeneca. All of these trials are part of the Galaxy Program, which has a three-fold objective. The first phase is to establish the LDL efficacy relative to other statins. We have a number of trials in a number of high-risk populations where we compare ourselves to other statins. Our LDL lowering is superior to the other statins. The second phase is testing the hypothesis that the best changes in LDL and HDL will translate into the best changes in atherosclerosis based on imaging. The ASTEROID trial was a study looking at regression of atherosclerosis. We have demonstrated significant reductions across all of our end points and we are the only statin monotherapy to do that. Atorvastatin and pravastatin have shown reductions in one of their end points, but we have shown regression in all three. Phase three is our clinical trial program is investigating mortality and morbidity using rosuvastatin. Those trials are ongoing and we are awaiting events. Crestor has quite a bit of data regarding renal disease. One of our mortality trials is

specifically investigating end stage renal disease of patients on dialysis. Crestor is currently on the PDL and we hope it remains there.

Dr. David Gross: Last year I talked in detail about many landmark studies involving Lipitor. The CARDS trial, diabetic patients without a history of CHD events or high elevations in cholesterol, showed a 37% reduction in cardiovascular events and a 48% reduction in the risk of stroke while using a low dose of Lipitor. The ASCOT study was in the hypertensive population using Lipitor 10 milligrams in hypertensive patients without a history of CHD or highly elevated cholesterol. We saw a 36% reduction in the primary endpoints at non-fatal MI and fatal CHD. The PROVE-IT trial looked at high dose Lipitor versus standard dose Pravachol. There was a significant difference in the aggressive therapy with Lipitor, 25% relative risk reduction in death and a 16% relative risk reduction in the primary endpoints of the study. The TNT trial looked at 10,000 patients over five years and the relative rate of major cardiovascular events comparing high and low doses Lipitor. There was no significant difference in terms of side effect outcomes. Lipitor now has an indication for the reduction of stroke, which was not the case the last time you reviewed this product. There is a lot of data across the dosage range for Lipitor. At the higher dose of 80 milligrams, we have studies showing the safety of the high dose. The KAPISH trial looked at conversion of people from simvastatin to atorvastatin. Those switched from simvastatin to Lipitor showed no signs of myosidis or symptomatic increases.

Dr. Carlson asked what the absolute risk reduction was. Dr. Gross was not certain, but he thought it was about 27. Dr. Maciejewski asked about statins, Lipitor in particular, having inflammatory properties beyond lowering of LDL. Dr. Gross said there was no definitive answer. In the PROVE-IT study, Lipitor significantly reduced LDL and HSCRP. Nothing can be concluded from this, because the dosages were not the same. People are now working on studies to answer this question.

Dr. Sater gave the First Health review of statins. There are six available entities. Both pravastatin and lovastatin are available in immediate and extended release formulations. There are three combination products: Advicor, Vytorin and Caduet. There are three high potency agents: atorvastatin, lovastatin and simvastatin; and three regular potency agents: pravastatin, fluvastatin and Lovastatin. They are considered clinically equivalent up to about 30% LDL reduction. All agents are indicated for the treatment of hyperlipidemia. In August, in Alaska, there were 1,665 claims for statin agents. The market share among the high potency agents is: generic simvastatin, 41%; ZoCor, 22%; Crestor, 17%; and Lipitor, 19%. Crestor and ZoCor are currently preferred. The market share among the low potency agents is: generic lovastatin, 43%; generic pravastatin, 37%; Pravochol, 13%; and Lescol, 7%. Currently, Altoprev, Lescol, Lescol XL and lovastatin are preferred. The market share for combination agents are: Vytorin, 93%; Caduet, 7%; and one claim for Advicor. Currently, Advicor and Vytorin are preferred. In previous discussions there was extensive conversation about evolving safety issues and the limited use of the low or regular potency agents in this class. The motion passed was that it was a class effect, however preferentially including one high potency statin, or two if Crestor ended up being the preferred agent due to Crestor safety concerns. Since the last review, generic simvastatin and pravastatin are available. There were a large number of expert letters submitted.

Dr. Demain noted that there no longer appeared to be any safety concerns with Crestor versus the other agents.

Dr. Carlson said while 90% of patients achieve their number goal on relatively small amounts of medication, 10% of the patients are more challenging to treat, so both the lower and higher potency

drugs are needed. The Veterans Administration has simvastatin as their chosen agent, but allows a higher potency agent for patients who fail to meet their goals.

Dr. Brodsky said he was unclear why so many of the physicians who wrote letters preferred Lipitor. Dr. Maciejewski said Lipitor has published extensive research and data. They are adding new indications for stoke, pediatrics, renal patients and others. He was not sure why they were interested in the low potency statins. In treating patients, he preferred to use a low dose of high potency statin versus a high dose of low potency statin.

Dr. Sater said there were 1,420 claims for high potency statins, 76 for low potency and 169 for the combinations. Dr. Maciejewski noted that within the high potency statins, Zocor was the least potent.

Dr. Bergeson pointed out that Zocor was now available as a generic. Dr. Sater said there were no supplemental rebates on generics, so sometimes the brand name was more cost beneficial.

Unidentified female said there might be an advantage to being somewhat consistent from year to year so medications do not have to be changed, which would require additional costs in lab work.

Dr. Briggs said there were benefits to including Provastatin, even though it is a low potency statin, for drug interactions or patients who have myalgia. Dr. Demain said a study showed that pravastatin probably had a greater risk of morbidity than the simvastatins. Dr. Hunt said there were risks in trying to lower LDL no matter what drug was used. It appears that Vytorin has fewer side effects, but has the same LDL reduction. Our first line goal is to reduce LDL cholesterol. We can usually get to goal using one of the three high potency agents.

DR. BRIGGS MOVED THAT THE THREE HIGH POTENCY AGENTS ARE A CLASS EFFECT AND THAT LIPITOR, CRESTOR OR ZOCOR BE INCLUDED ON THE PDL. SECONDED BY DR. STRANSKY.

Dr. Hunt felt the term "class effect" was being used too loosely. He felt they should be more precise in defining exactly what effect they were looking for. Dr. Brodsky said in the statin class they were looking to lower lipid levels and the outcome of reduced cardiovascular disease. The overall goal is a reduction in mortality and morbidity related to cardiovascular disease. Dr. Hunt felt they should be clear about what effect they were looking for. The board discussed the term "class effect."

DR. DEMAIN MOVED TO AMEND THE MOTION TO INCLUDE EITHER SIMVASTATIN OR ROSUVASTATIN ON THE PDL. THERE WAS NO SECOND.

The board further discussed the term "class effect." Dr. Carlson said class effect meant there was no convincing evidence to show that one drug was super superior over another. Dr. Hunt felt the committee should agree on what they were looking for within a certain class. Dr. vonHafften said referring to drugs as a class effect or therapeutically equivalent can imply that they are interchangeable and we need to be careful about that. Dr. Brodsky said studies looked at a majority of patients, but there would always be exceptions. Patients who do not respond, or have adverse effects to a drug, can be prescribed any medication by writing "medically necessary" on the prescription. Dr. Demain felt they should be looking at the drug as a whole to determine if it is significantly preferred. If it is not significantly preferred, it can be considered equivalent. We do not have that data on Crestor. Dr.

Conright felt the committee needed to consider on what class effect they were agreeing to when deciding drugs are equivalent.

THE MOTION PASSED WITH TWO OPPOSED.

11. Re-review of Opioids, Long Acting

Dr. Brodsky noted that this class had been previously reviewed, but no action had been taken.

There was no public comment on this class.

Dr. Sater gave the First Health review of Opioids, Long Acting. There are three available entities. We will discuss four oral morphine dosage forms. All are MU receptor antagonists with the same mechanism of action, similar efficacy and side effect profiles. Pharmacokinetic parameters different between products. Many products carry a black box warning regarding extreme potency, abuse potential and over dose of patients. In August, in Alaska, there were 470 claims for drugs in this class: oxycodone sustained release, 30%; transdermal fentanyl, 24%; OxyContin, 15%; Kadian, 14%; Avinza, 12%; Duragesic, 3%; and MS Contin and Oramorph each had 1%. Avinza, Duragesic, Kadian, extended release morphine, Oramorph and OxyContin are currently preferred. Previous discussion occurred in September 2004. There was significant discussion about inter patient viability as related to the different drugs and preparations. There have been few changes since that time, although some generics have been added to the class. Dr. Polston will give the expert opinion.

Dr. Brodsky asked about the prior authorization issues in this class. Dr. Sater said prior authorization would be required for all drugs in this class. The committee discussed the prior authorization requirements. There are certain overrides, such as for cancer patients or long-term hospice patients.

Dr. Sater noted that the committee would be discussing all of the drugs, except for Actiq.

Dr. Polston discussed the drug class. (Indiscernible -- away from microphone.) Over the last three months the following drugs were prescribed: methadone, 40%; morphine, 25%; fentanyl, 20%; and OxyContin, 10%. There are some real controversies in prescribing these medications, because there is no clear way to gauge pain. I look at the patient's outcome when using these medications. It really becomes a question of what are the class effects and outcomes. As we get into higher doses, we are starting to see evidence that the patient's pain tolerance actually goes down. In non-malignant pain, continuously increasing the doses is not appropriate if you are not seeing any improvement in functions.

Dr. Brodsky asked if it was better to put people using short-term drugs on long-term drugs. Dr. Polston said there was evidence that continuous dosing of pain medication lowers the total dose a patient receives. There is also a theory that using long acting agents decreases tolerance, but there is no evidence to indicate that it increases or changes tolerance. I have some patients on short acting medicines for long periods of time without any difficulties at all. There are patients that rapidly get tolerant to these medications, so it is a very difficult thing to assess. It is also difficult to determine if the patient's tolerance is increasing or if there are other factors affecting the patient that causes them to report more pain. At least one of these agents should be included on the PDL.

Dr. Brodsky said he was pleasantly surprised by the low use of OxyContin. Dr. Polston said physicians are now very concerned about prescribing OxyContin. There may be some evidence that it has a higher addiction potential, but that is not clearly defined. OxyContin is an excellent drug, but I do not use it as a first line drug. There are a lot of pharmacies that no longer stock OxyContin.

Dr. Richey asked why so many of these drugs were on the PDL when there was no clear evidence that one was better than the other. Dr. Brodsky said the previous decision was this was a class effect. Since the prices were remarkably close, many of them ended up on the PDL.

DR. POLSTON MOVED THAT THE LONG-ACTING AGENTS WERE A CLASS EFFECT, BUT ACTIQ SHOULD NOT BE INCLUDED. SECONDED BY DR. BERGESON.

Dr. Briggs asked what were the differences between the morphine products. Dr. Polston said he had noticed no consistent difference within the class. Avinza has a once daily dosage, but some patients prefer to actively treat the pain and prefer a more frequent dosing schedule. Kadian seems to be well tolerated by patients who cannot tolerate other drugs in the class.

Dr. Miller asked about OxyContin, the brand versus the generic. Dr. Polston said OxyContin became a popular, top shelf drug to take. There may be something unique about OxyContin that makes it more addicting, but I'm not convinced of that.

DR. LILJEGREN MOVED TO AMEND THE MOTION TO INCLUDE AT LEAST ONE ORAL MEDICATION ON THE PDL. SECONDED BY MS. STABLES.

THE AMENDMENT TO THE MOTION PASSED WITH ONE OPPOSED.

THE MOTION PASSED UNANIMOUSLY.

12. Re-review of Bisphosphates

Dr. Frank Wollaeger: At the last review, I spoke about the efficacy of Boniva including reduction of vertebral fractures by 52% over three years and a reduction in non-vertebral factures of 69% in high-risk patients. In patients with a lumbar spine T-score of -2.5 or lower, and a history of clinical fractures in the previous five years, a significant 60% reduction in non-vertebral fractures was seen. Although no head-to-head Boniva studies have been completed, these results are consistent with the bisphosphates class. Once monthly Boniva is different than other bisphosphates, because of its unique chemical structure. Boniva can be given at higher doses, less frequently, providing the expected anti-receptive efficacy with a lower cumulative monthly dose of bisphosphate. Boniva is the only bisphosphate that demonstrates superior BMD gains when compared to its daily regimen. The extended dosing efficacy trial called the MOBILE trial demonstrated continuous yearly increases in lumbar spine BMD to 6.6% and total hip BMD to 4.2%. Boniva has demonstrated its safety, as well as its efficacy. In the MOBILE study, the daily 2.5-milligram dose was compared with the monthly 150-milligram regimen. The frequency of upper GI adverse events was comparable in both groups. Additionally, the incidents of all adverse events were similar in both groups. Patients prefer drugs that are given less frequently. In a preference study comparing once monthly Bovina to once weekly

Fosamax, 66% of patients preferred once monthly Boniva. Study participants indicated that it would be easier to follow the regimen over the long-term and that the regimen fit their lifestyle better. Medication adherence is critical to insuring positive patient outcomes. Studies show that 50% of patients fail to continue once weekly bisphosphate after only a year. This is important, as the data indicates that patients who do not comply and/or persist on therapy have a significantly higher risk of fractures, greater hospitalization rates and higher medical costs. In a recent preference trial, patients were asked why they preferred once a month therapy. Their reasons included that GI discomfort, which is associated with the bisphosphate class, would be more tolerable than weekly. In a prospective study conducted in the UK, Boniva, coupled with a patient support program, produced a 47% improvement in persistence versus weekly Fosamax. Boniva is the only bisphosphate that makes a patient reminder program available via email, telephone or mail to help enhance compliance. Once monthly Boniva is a unique drug that patients prefer and find more convenient, which has lead to an increased persistence. If patients don't take the bisphosphate, they will be more likely to suffer future fractures, which will ultimately cause the State of Alaska more money.

Dr. Stransky asked if there was any bone density or fracture data on the monthly Boniva. Dr. Wollaeger said there was no fracture data on any bisphosphates on their extended dosing regimen. The studies are always bridging studies that compare the BMD to the BMD of the daily regimen.

Dr. Sater said the committee would only be discussing alendronate, ibandronate and risedronate today. The committee asked that in the future, the drugs to be discussed be indicated in the information.

Dr. Sater gave the First Health presentation on bisphosphates. Of the three oral bisphosphates, two are available in combination. They have similar adverse event profiles. Boniva is given once a month. Actonel and Fosamax are most commonly given once a week. In August, in Alaska, there were 195 claims. All formulations of Fosamax are preferred. The following market share was reported: Fosamax tablets, 73%; Fosamax Plus D, 9%; Fosamax solution, 4%; Actonel tablets, 17%; Actonel calcium, 1%; and Boniva, 5%. The previous discussions centered on the significance of bone marrow density, surrogate markers of bone turnover and fracture rates. A motion was made to insure that a weekly or monthly preparation, not a daily preparation, be included. A class effect was declared. I do not have any pediatric data on bisphosphates.

Dr. Brodsky said they were mainly looking for the treatment of osteoporosis. Dr. Conright asked if they were looking at bone density or fractures. Dr. Stransky said bone density goes down over time and the fracture rate is directly proportional to the combination of age and bone density. There is some discussion whether architecture has a lot to do with it, but you need a bone marrow biopsy in order to prove it. There is a lot of correlation between bone density and fractures. All three products have effectively increased bone density and decrease fracture rates. Fluorides have been shown to increase bone density, but fracture rates increase due to brittleness. Dr. Conright asked if bone density was the effect they were discussing and voting on. Dr. Sater said if the decision was based on fracture data then they would be limited to a daily dose product.

Dr. Hunt said the BMD data should be accepted for weekly or monthly products as acceptable proxies of fracture and outcome data in the bisphosphate class.

DR. HUNT MOVED THAT THE DRUGS BE CONSIDERED A CLASS EFFECT AND AT LEAST ONE LONG ACTING PRODUCT BE INCLUDED ON THE PDL. SECONDED BY AN UNIDENTIFIED MALE.

THE MOTION PASSED UNANIMOUSLY.

13. Other Business

Dr. Sater referenced the DUR report. Questions or suggestions are welcome. Dr. Polston asked if there was any statewide data on adverse drug consequences that is usable as a baseline for picking subjects. Mr. Campana said he would review the data.

Dr. Sater discussed the cost savings report. The supplemental rebates are $2.90 saved per claim, which averages out to about a $220,000 saving per month. Dr. Brodsky noted that Medicare Part D really cut down on the savings that he had anticipated.

14. Approval or Prior Minutes:

Dr. Brodsky asked for comments on the meeting minutes May 19, 2006.

- Mr. Campana said the first public comment was probably Dr. Woodard instead of Dr. Bergstrom.
- Dr. Demain said the final paragraph on page 8, regarding genetic markers, should be ARG:ARG instead of ART.

DR. BERGESON MOVED TO ACCEPT THE MINUTES AS AMENDED. SECONDED BY DR. STRANSKY.

THE MOTION PASSED UNANIMOUSLY.

15. Final Comments by Chair or Other Members

Dr. Brodsky said that Drs. Stransky, Boothe, vonHafften and Mr. Miller would be leaving the committee. Mr. Campana thanked the four members for their work and presented each with a certificate of appreciation. Dr. vonHafften's replacement will be Lucy Curtis from the Anchorage Community Mental Health Clinic. No other replacements have been found. Recommendations are welcome.

Dr. Campana said the honorarium was being discussed. There has been a change in IRS regulations. You will now have to sign in at each meeting. Those on teleconference will be noted, but may have to do something else to verify attendance. Dr. Demain asked if there was a way to sign an honorarium directly over to a charity. Mr. Campana did not believe that option was currently available.

Dr. Sater reviewed the changes made to the PDL at this meeting.

- Alpha Blockers for BPH: Flomax and Uroxatral, in addition to generic terazosin and doxazosin, will be preferred.
- Androgen Hormone Inhibitors: Avodart and Proscar will be preferred. Generic finasteride will be non-preferred for now.
- Electrolyte Depletors: All three agents will be preferred.
- Lipotropics - Fibric Acid: Generic gemfibrozil and Lofibra will be preferred.
- Lipotropics - Niacin: Niaspan will be preferred.
- Zetia will be retained on the PDL.
- Statins: Advicor, Lescol, Crestor, Vytorin and Zocor will be preferred. Generic simvastatin will be non-preferred at this time.
- Long-Acting Narcotics: Duragesic, Kadian, generic morphine sulfate, and Oramorph will be preferred.
- Bisphosphates: All formulations of Fosamax will be preferred.

Dr. Hunt said the website needed to be upgraded. It is awkward to open a PDF and find a drug class, because they are not always consistently named. It would be great to be able to search for information in an HTML type of format. Mr. Campana noted that a search could be done on a PDF by using the "spyglass" at the top of the page.

Dr. Sater reviewed the topics for the next meeting, which will be October 13, 2006.

DR. BRIGGS MOVED TO ADJOURN. SECONDED BY DR. STRANSKY.

THE MOTION PASSED UNANIMOUSLY.

The meeting adjourned at 11:09 a.m.